REMARKS

The present application was filed on July 10, 2003 with claims 1 through 21. Claims 2, 6, 10-13, 16 and 18 have been previously canceled without prejudice. Claims 10-13 had been withdrawn from consideration in response to a restriction requirement. Therefore, claims 1, 3-5, 7-9, 14, 15, 17 and 19-21 are presently pending in the above-identified patent application. Applicant herein proposes to amend claims 1, 14 and 21. Support for the amendments can be found, for example, on page 11, lines 11-13 and page 12, lines 18-20, and page 8, lines 1-7 and page 9, lines 14-18. No new matter is being introduced.

In the Office Action, the Examiner rejected claims 1, 3-5, 7-9, 14-15, 17 and 19-21 under 35 U.S.C. §101 because the claimed invention is allegedly directed to non-statutory subject matter, rejected claims 1, 3-5, 7-9, 14-15 17 and 19-21 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, and rejected claims 1, 3-5, 7-9, 14-15, 17 and 19-21 under 35 U.S.C. §103(a) as allegedly being unpatentable over Eisenberg et al. (Nature, volume 299, 1982, pages 371-274) (hereinafter "Eisenberg") in view of Silverman (PNA; April 24, 2001; volume 98, pages 4996-5001) (hereinafter "Silverman").

The comments of the Examiner in forming the rejections are acknowledged and have been carefully considered.

Section 101 Rejection

In the Office Action, the Examiner rejected claims 1, 3-5, 7-9, 14, 15, 17 and 19-21 under 35 U.S.C. §101 as allegedly being directed to non-statutory subject matter. Specifically, the Examiner stated on page 5 of the Office Action that

> ...the method to be performed does not produce a tangible result. For example, the method as claimed may take place entirely within the confines of a computer without any communication to the outside world and without using or making available for use, the results of the computation to a "user" (i.e. one performing the method)....
>
> Applicant argues that the amendments "outputting the global linear hydrophobic moment to at least one of a user, a display, a memory and one or more additional computers on a network," overcome the 35 U.S.C. 101 rejections. This is not found to be persuasive because this amendment still yields nonstatutory embodiments. For example, outputting results to a memory may yield a result that is only accessible to another computer and not a result that is tangibly accessible to a user.

Applicant, as proposed herein, has amended independent claims 1, 14 and 21 to include the limitation of outputting the global linear hydrophobic moment to at least one of a user, a display and one or more additional computers on a network. Support for the amendment can be found, for example, on page 11, lines 11-13 and page 12, lines 18-20. As such, Applicant respectfully asserts that the amendment overcomes the aspect of the rejection noted above.

Therefore, Applicant respectfully asserts that independent claims 1, 14 and 21, as amended, overcome the §101 rejection. Also, Applicant further submits that by virtue of their dependence on allowable independent claims 1 and 14, claims 3-5, 7-9 and 15, 17-20, respectively, are directed to statutory subject matter in their own right.

Thus, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1, 3-5, 7-9, 14, 15, 17 and 19-21 under 35 U.S.C. §101.

Section 112, Second Paragraph Rejection

In the Office Action, the Examiner rejected claims 1, 3-5, 7-9, 14, 15, 17 and 19-21 under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to

particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner stated on page 6 of the Office Action that

> [i]n claims 1, 14 and 21, it is unclear how the correlation enhancing step relates to the remainder of each of the claims. For example, in claim 1, in the steps of "enhancing correlation between residue centroid magnitude and residue solvent accessibility, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric," both solvent accessibility and this enhanced correlation are not referred to in subsequent steps of the claim.

Applicant has amended independent claims 1, 14 and 21 to include the limitation of using the first-order hydrophobic moment and the enhanced correlation between residue centroid magnitude and residue solvent accessibility to define the global linear hydrophobic moment, wherein each of the residue centroids contributes a magnitude and direction to the global linear hydrophobic moment. Support or the amendments can be found, for example, on page 8, lines 1-7 and page 9, lines 14-18.

As such, Applicant respectfully asserts that the amendment overcomes the rejection. Also, Applicant further submits that by virtue of their dependence on allowable independent claims 1 and 14, claims 3-5, 7-9 and 15, 17-20, respectively, are patentable in their own right. Thus, Applicant respectfully requests reconsideration and withdrawal of the rejection of claims 1, 3-5, 7-9, 14, 15, 17 and 19-21 under 35 U.S.C. §112, second paragraph.

Section 103(a) Rejection

The Examiner also rejected claims 1, 3-5, 7-9, 14, 15, 17 and 19-21 under 35 U.S.C. §103(a) as allegedly being unpatentable over Eisenberg in view of Silverman.

On page 10 of the outstanding Office Action, the Examiner stated that

> Eisenberg et al. does not use residue centroids as the origins in the hydrophobic moment calculations..., Eisenberg et al. does not show correlation enhancement between residue centroid magnitude and solvent accessibility....
>
> In equations [13] and [14] on page 4998 of Silverman, distance metrics, ellipsoidal metrics, and a solvent accessibility are all used to enhance the centroid magnitude.

Applicant respectfully traverses the Examiner's rejection. Specifically, Applicant respectfully asserts that the metrics taught in Silverman (and cited by the Examiner) are only applied to second- and zero- order moments. As taught and claimed herein, a calculation of a first order moment (the hydrophobic dipole) of an arbitrary structure is performed, and a correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric in an effort to define the global linear hydrophobic moment. Applicant respectfully asserts that a first-order moment is completely different from a zero- and/or a second-order moment.

Applicant points to page 5001, left column, of the Silverman reference, wherein it is stated that

> [t]his paper has focused on the spatial region of transition between the hydrophobic core and hydrophilic exterior of globular proteins. The moment calculations have identified two features, apparently independent of protein size and fold, that are comparable for the 30 protein structures obtained from the PBD and for the 14 native structures of the decoy set. One, a global feature, is the overall shape or profile of the second-order ellipsoidal moment calculated from protein interior to exterior. The other, a specific features, the hydrophobic ratio, is the ratio of distances at which the second- and zero-order moments of the distribution vanish. (Emphasis added).

Applicant also highlights the present specification, beginning on page 8, line 1, wherein it is stated that

> [t]he correlation between residue centroid magnitude and residue solvent accessibility is enhanced, as shown in step 106 of FIG. 1. An exemplary embodiment for enhancing the correlation between residue centroid magnitude and residue solvent accessibility is described below in conjunction with the description of FIG. 2. Thus, when defining the global linear hydrophobic moment, each residue centroid contributes a magnitude and direction to the global linear hydrophobic moment, as shown in step 108 of FIG. 1. Further... each residue centroid having the same fractional distance to the surface of the tertiary protein structure will contribute an equivalent magnitude of the global linear hydrophobic moment. An accurate determination of the magnitude of the global linear hydrophobic moment is important.... Therefore, one feature that should be modified in Equation 3 [first-order hydrophobic moment] is the lever arm dependence of each hydrophobic moment.... As can be seen in FIG. 2, a residue near the exterior of a protein and also near the major principal axis is at a

> greater distance from the center of the protein than a residue near the exterior of the protein but near the minor principal axis.... Even though the two residues are at the same fractional distance to the protein surface, the distance from the origin is different. The two residues would therefore make different contributions to the magnitude of the vector... in Equation 3. This difference can be corrected based on a spatial linear moment of each residue by mapping the ellipsoidal coordinates onto a sphere with radius equal to the major principal axis.... Since each residue then has an approximately equivalent magnitude, it may be assumed that they contribute an equal magnitude to the global linear hydrophobic moment. With this mapping, Equation 3 is written as [Equation 10]....

As a result, Applicant respectfully asserts that even if properly combined, the above-cited references do not teach or suggest all of the claimed limitations of independent claims 1, 14 and 21. The references do not teach or suggest calculating a first-order hydrophobic moment, enhancing correlation between residue centroid magnitude and residue solvent accessibility, wherein the correlation between residue centroid magnitude and residue solvent accessibility is enhanced using a distance metric, using the first-order hydrophobic moment and enhanced correlation between residue centroid magnitude and residue solvent accessibility to define the global linear hydrophobic moment, wherein each of the residue centroids contributes a magnitude and direction to the global linear hydrophobic moment, and using the global linear hydrophobic moment to characterize an amphiphilicity of a tertiary protein structure.

Therefore, all of the claimed limitations of claims 1, 14 and 21 are not taught or suggested by the prior art, and as a result, Applicant respectfully asserts that amended independent claims 1, 14 and 21 overcome the rejection as allegedly unpatentable over the references cited in this rejection. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

Also, Applicant further submits that by virtue of their dependence on independent claims 1 and 14, claims 3-5, 7-9 and 15, 17-20, respectively recite patentable subject matter in their own right. If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *In re Fine*, 837 F.2d 1071, 5 USPQ2d

1596 (Fed. Cir. 1988). Therefore, Applicant respectfully requests withdrawal of the §103(a) rejection from claims 1, 3-5, 7-9, 14, 15, 17 and 19-21.

All of the pending claims, i.e., claims 1, 3-5, 7-9, 14, 15, 17 and 19-21, are in condition for allowance and such favorable action is earnestly solicited.

If any outstanding issues remain, or if the Examiner has any further suggestions for expediting allowance of this application, the Examiner is invited to contact the undersigned at the telephone number indicated below.

The Examiner's attention to this matter is appreciated.

Respectfully submitted,

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Michael J. Cooper
Attorney for Applicant(s)
Reg. No. 57,749
Ryan, Mason & Lewis, LLP
1300 Post Road, Suite 205
Fairfield, CT 06824
(203) 255-6560